

EXHIBIT B8

Biologic Plausibility: Chronic Inflammation

"With respect to talc specifically, local irritation leading to an inflammatory response is one of the possible mechanisms of tumour progression that is frequently hypothesized. (Draft Screening Assessment, Talc, Environment and Climate Change Canada, Health Canada, December 2018, p.18)

"There is support for an association of inflammation and increased risk of ovarian cancer." (Draft Screening Assessment, Talc, Environment and Climate Change Canada, Health Canada, December 2018, p.18)

"Chronic inflammatory response and alteration in local immunogenicity are possible mechanisms. (Taher 2018, *unpublished*, p. 26)

"If chronic inflammation due to ascending foreign bodies is indeed the mechanism by which talc is associated with increased ovarian cancer, then these results fit the picture." (Penninkilampi 2018, p. 45)

"Epidemiologic evidence implicates chronic inflammation as a central mechanism in the pathogenesis of ovarian cancer, the most lethal gynecologic cancer among women in the United States." (Trabert, Pinto, Hartage, et al, 2014, p. 2)

"Our study provides additional evidence that inflammation plays an important role in ovarian carcinogenesis." (Trabert, Pinto, Hartage, et al, 2014, p. 13)

"Our findings on talc and endometriosis are consistent with previous findings and are compatible with the hypothesis that these factors increase the risk of ovarian cancer and that inflammation may be a common pathway." (Wu 2009, p. 6)

"Chronic inflammation has been proposed as the possible causal mechanism that explains the observed association between certain risk factors, such as use of talcum powder (talc) in the pelvic region and epithelial ovarian cancer." (Merritt, 2008, p. 170)

"Chronic inflammation...was first invoked as a possible mechanism leading to the development of epithelial ovarian cancer to explain observed associations between certain factors, such as talcum powder in the perineal region or pelvic inflammatory disease (PID) and risk of ovarian cancer." (Merritt, 2008, p. 170)

"Indeed the most consistent evidence linking inflammation with ovarian cancer comes from the many reports that use of talc in the perineal region increases ovarian cancer risk." (Merritt, 2008, p. 170)

"Talc particles can induce an inflammatory response *in vivo*, which may be important in ovarian cancer risk. Normal ovarian cells treated with talc are more likely to undergo cell proliferation and neoplastic transformation, and cellular generation of reactive oxygen species increases with increasing exposure to talc." (Gates, 2008, p. 8)



“The mechanism of carcinogenicity may be related to inflammation.” (Langseth 2008, p. 360)

“Collectively, these studies point to a possible etiologic role of talc in ovarian cancer via an inflammatory process at the site of the ovarian epithelium” (Mills 2004, p. 458)

“Inflammation involves rapid cell division, DNA excision and repair, oxidative stress, and high concentrations of cytokines and prostaglandins, all of which are established promoters of mutagenesis.” (Ness 2000, p. 111)

“At the same time, a growing body of epidemiologic evidence suggests that factors causing epithelial inflammation are involved in ovarian carcinogenesis. Such factors include asbestos and talc exposures, endometriosis and pelvic inflammatory disease (PID).” (Ness 1999, p. 1459)

“Inflammation by its nature, produces toxic oxidants meant to kill pathogens. These oxidants cause direct damage to DNA, proteins and lipids and may, therefore play a direct role in carcinogenesis. (Ness 1999, p. 1463)

“Direct induction of inflammation as a result of endometriosis, talc and asbestos exposure, and PID, as well as ovulation itself, may act to promote ovarian tumorigenesis.” (Ness 1999, p. 1459)

“We have reviewed the data suggesting that an additional mechanism that may underlie ovarian cancer is inflammation, with concomitant rapid DNA turnover and defective repair.” (Ness 1999, p. 1464)